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GENES, VEGETABLES, RESIDENTIAL RADON AND RISK OF LUNG CANCER IN NON-SMOKING WOMEN

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Background: Vegetable intake may reduce lung cancer risks by 40% in smokers with homozygous deletion of GSTM1(GSTM1*0)[Lancet 356:724,2000]. The protective effect may come from isothiocyanates that induce Phase 2 detoxification enzymes. Since GSTM1 hastens isothiocyanate removal, an inherited deficiency may enhance detoxification in habitual vegetable consumers.

Hypothesis: Current models focus on neutralizing chemical carcinogens. However, tobacco smoke also contains ^{210}Po, which produces an α-particle on decay, and phase 2 enzymes defuse many toxins including reactive oxygen species (ROS) produced by α-particles. We propose that vegetables speed ROS detoxification by inducing phase 2 enzymes. To test this model, we examined lung cancer risks in never-smokers exposed to residential radon because ^{222}Rn produces an α-particle during its radioactive decay.

Methods: Gene-environment interactions were calculated using cases only. Germline DNA samples from 106 never-smokers with lung cancer were genotyped for GSTM1 status. Vegetable intake was determined from questionnaire information; and radon concentrations were measured in air samples.

Results: Compared to never-smokers exposed to the lowest tertile of radon (<1 piC/L), those with GSTM1*0 and the highest tertile of radon exposure (>2 piC/L) had no increased risk (OR=1.3,95%CI=0.4-4.1). But notable trends emerged when GSTM1*0 and radon were stratified by vegetable intake: less than mean consumption increased risk (OR=4.2, 95%CI=0.6-31.4) while more than mean ingestion reduced risk (OR=0.4, 95%CI=0.08-2.4).

Conclusions: These pilot data suggest that frequent vegetable consumption and deficient GSTM1 enzymatic activity may mitigate cancer risks from exposure to radon gas.

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RISK OF COLORECTAL CANCER DUE TO ALCOHOL CONSUMPTION AT THE LOWER VITAMIN INTAKES. A HOSPITAL-BASED CASE-CONTROL STUDY IN POLAND.

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The purpose of the study was to assess the relation between simultaneous exposure to alcohol and consumption of micronutrients that may have protective property against colorectal cancer. The hospital based case-control study of colorectal cancer has been carried out between January 1998 and November 1999 in Krakow, Poland. In total, 180 incident cases of colorectal cancer confirmed by histopathology were recruited from the University Hospital in Krakow. The equal number of controls individually matched by gender and age (+/-5 years) were chosen amongst patients with no history of cancer from the same hospital. Food frequency questionnaire for 148 food items combined with quantity of foods eaten was used to assess the usual dietary pattern. The data confirmed the inverse association between intake of retinol, thiamine or antioxidant micronutrients (vitamin C and E) and the occurrence of colorectal cancer. Alcohol intake appeared to be an important risk factor for this cancer site and the risk increased with the amount of pure alcohol intake. The group with lower intakes of retinol, caroten, vitamin C, and E, but with higher consumption of alcohol run a noticeably high risk of colorectal cancer (OR=6.79; 95%CI: 2.08-22.18). However, the risk was markedly lower among those alcohol drinkers who reported high intake of micronutrients (OR=1.35; 95% CI: 0.39-4.67). The data suggest that higher consumption of alcohol, when combined with low intakes of retinol and antioxidant vitamins may considerably increase the risk of colorectal cancer.

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REPEATABILITY OF QUESTIONNAIRE DATA ON CHILDREN'S RESPIRATORY SYMPTOMS AND INDIVIDUAL RISK FACTORS.

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A Cross-sectional study was conducted in the Russian Federation to analyze the association between air pollution characteristics of 9 cities and the prevalence of children's respiratory symptoms in them. Within the framework of this study, we analyzed the repeatability of questionnaire data. In the cities of Verkhnyaya Pyshma, Sverdlovsk Region, and Cherepovets, Vologda Region, we distributed self-administered questionnaires twice. The questionnaires were handed out by schoolteachers in class and then filled in by an adult relative of the child at home. Thus, there was no direct communication between the researcher and the respondent. We carried out the repeatability analysis to assess the reliability of the data collected in this manner. 353 schoolchildren from Verkhnyaya Pyshma and 107 from Cherepovets, a total of 460, participated in both studies. The first survey (in the framework of a pilot study) was conducted in November 1998 and the second survey (the main study) - in May 1999. We assessed the repeatability of questions about respiratory health (kappa ranging 0.29 - 0.67, reflecting in part real changes in symptoms from November to May) and individual risk factors (kappa 0.43 - 1). We found no considerable differences in the repeatability of answers between the two areas. We also examined the reproducibility of responses depending on the person filling in the questionnaire. The results were the best if the mother filled in the questionnaire in both surveys and the worst if the respondents differed. We assessed how the repeatability depended on defining the analyzed variables which helped us choose the best way of selecting the summary variables for analysis.

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CYTOKINE POLYMORPHISMS PLAY A ROLE IN THE SUSCEPTIBILITY FOR UVB-INDUCED IMMUNOMODULATION AFTER HEPATITIS B VACCINATION IN HUMAN VOLUNTEERS

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UVB exposure (280-320 nm) impairs specific and non-specific immune responses. As responses to microbial agents can be affected, it has also been suggested that immune responses to vaccination may be affected. We have carried out a volunteer study in 129 human subjects to study the effect of suberythemal artificial UVB (TL 12 lamps) on hepatitis B vaccinations. The volunteers were exposed to UVB on 5 consecutive days (1 MED per day) followed by the standard hepatitis B vaccination protocol (0, 1 and 6 months, 20 µg, i.m., Engerix-B™). Although the UVB exposure regime was sufficient to suppress CHS responses and NK activity, antigen-specific humoral (antiHBs-Ig) and cellular immunity (proliferation induced by HBsAg) were not affected. We have determined single nucleotide polymorphisms (SNPs) for the following interleukins: IL-1RA (+2018), IL-1A (+4845), IL-1B (+3953), TNF-A (-308) and TNF-A (-238) from all volunteers. These polymorphisms quantitatively affect production of the corresponding interleukins. Taking these cytokine polymorphisms into account, it was demonstrated that the humoral and cellular immune responses to the hepatitis B vaccine as well as the susceptibility for UVB-induced immunomodulation depends on the type of polymorphism.

ISEE-256

STATISTICAL METHODS FOR THE SYNTHESIS OF EPIDEMIOLOGICAL AND TOXICOLOGICAL RESEARCH: CHLORINATED BY-PRODUCTS AND ADVERSE REPRODUCTIVE OUTCOMES

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Studies of environmental risk often need to combine epidemiological and toxicological data; this is usually done informally. This research is exploring quantitative methods to combine such data. A potential link between chlorinated by-products (CBPs) and adverse reproductive effects is used as an example. A systematic literature review identified over 70 relevant papers, which vary within and between disciplines. The epidemiological studies include many designs investigating a range of exposures (e.g. estimated CBP levels, water source) and outcomes (e.g. spontaneous abortion, birth weight). Reproductive outcomes (e.g. litter size, foetal weight) are common to most toxicological studies, but different animal species are used. The risk estimates (odds ratios (OR), mean number of observations) are also reported differently between the designs. Initially a possible link between low birth weight and exposure to trihalomethanes, the most commonly occurring CBPs, has been studied. To combine the data the reported results must be transformed to a common form. For example, a reported mean and SD of foetal weight from a toxicological study (e.g. at a dose of 126 mg/kg/day: mean=3.7, SD=0.4) can be transformed into an OR (of 7.33) for low foetal weight at that dose. This may then be combined with the ORs reported in the epidemiological studies. A hierarchical Bayesian framework for generalised synthesis of evidence methods (Prevost et al, 2000), is used to combine these data. This methodology helps to identify inconsistencies between the various pieces of evidence, and to identify areas in which more data are essential. Prevost TC et al (2000) Hierarchical models in generalised synthesis of evidence: an example based on studies of breast cancer screening. Stat Med,19, 3359-76

ISEE-257

BACKS TO THE FUTURE: REASSESSING DONORA AND LONDON

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Objective: 50 years after lethal episodes of air pollution in Donora and London, this paper provides new evidence on the full health impacts of these episodes. Methods: Using historical archives, indirect indicators of mortality and morbidity, and interviews with survivors, we recalculate the burden on public health from elevated levels of air pollution from acute and chronic impacts on morbidity and mortality. We close with personal reminiscences from Donora.

Results: We find that mortality and morbidity associated with acute episodes of air pollution is considerably higher than previous published estimates have indicated.

Discussion: Levels of acute air pollution that are estimated to have occurred during these lethal episodes can be found today in rapidly developing cities.

Conclusion: Lethal episodes of air pollution are a continuing public health problem and have been historically underestimated.